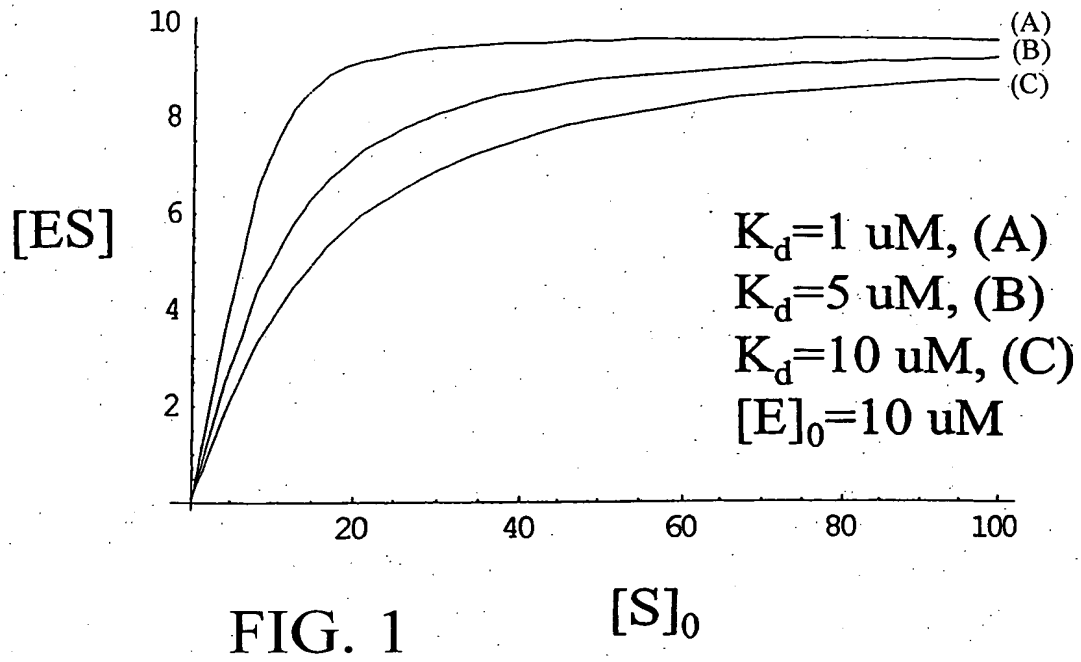

FIG. 1

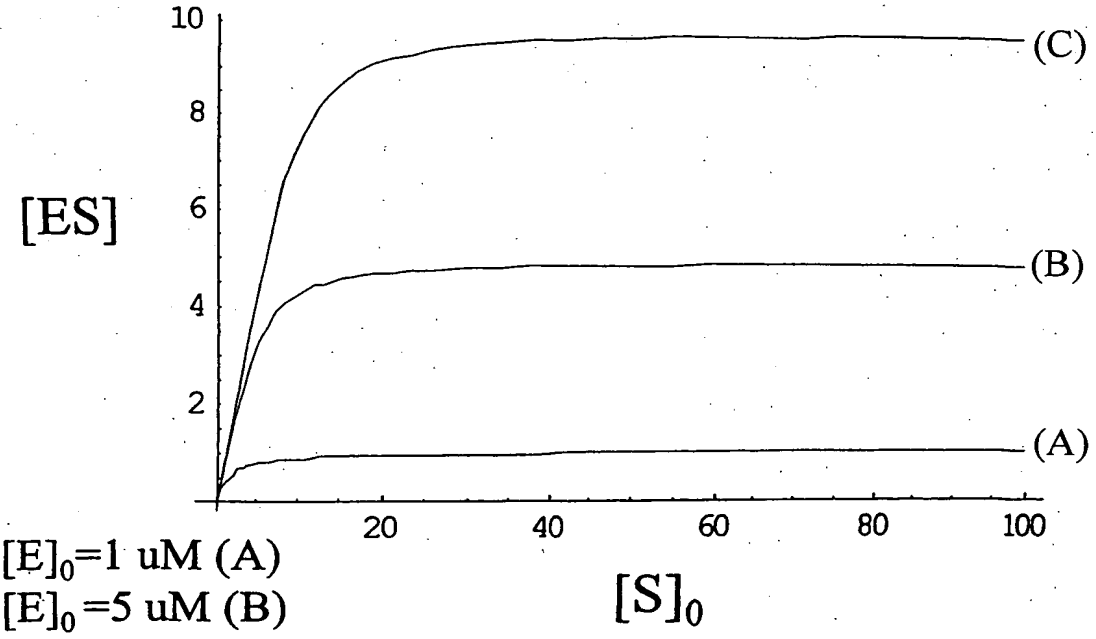

FIG. 2

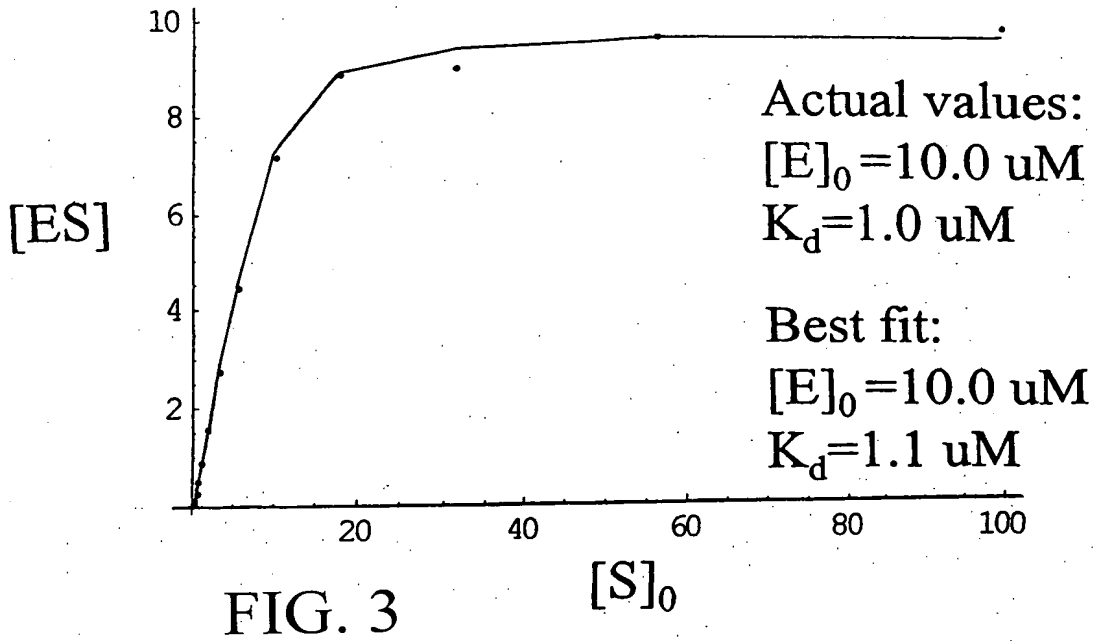

FIG. 3

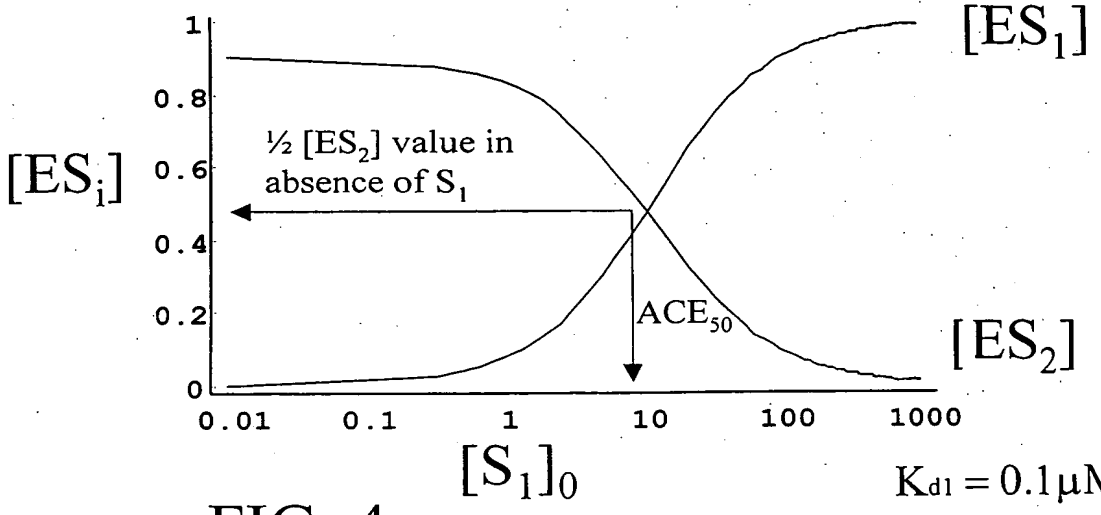

FIG. 4

$K_{d1} = 0.1\mu M$

$K_{d2} = 1.0$

$[S_1]$ = variable

$[S_2]_0 = 10$

$[E]_0 = 1$

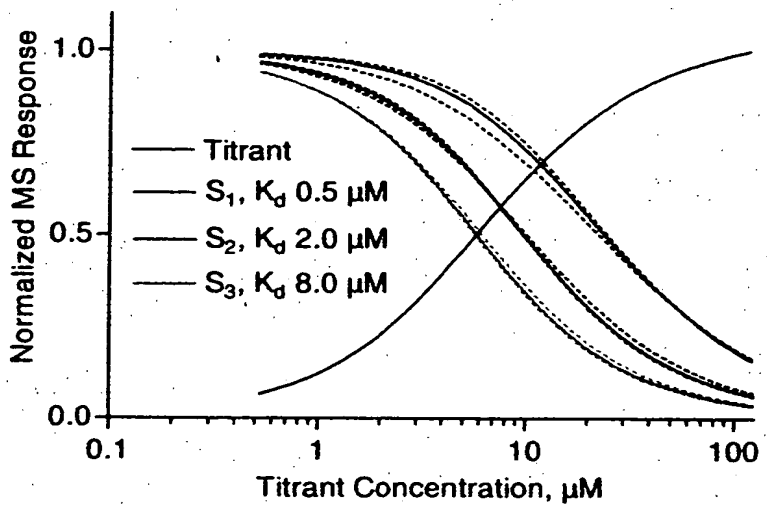
Normalized MS Response
1.0
0.5
0.0
0.1
1
10
100
Titrant Concentration, µM
Titrant
S1, Kd 0.5 µM
S2, Kd 2.0 µM
S3, Kd 8.0 µM

FIG. 5A

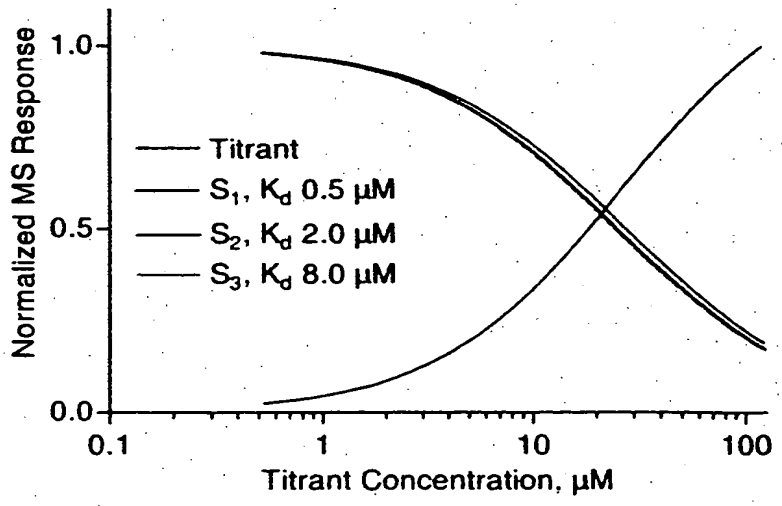
Normalized MS Response
1.0
0.5
0.0
0.1
1
10
100
Titrant Concentration, µM
Titrant
S1, Kd 0.5 µM
S2, Kd 2.0 µM
S3, Kd 8.0 µM

FIG. 5B

$$
\begin{aligned}
kd2 = {} & -(-4\,ace50^2 + 5\,ace50\,e0 - 2\,e0^2 + 2\,ace50\,kd1 - 4\,e0\,kd1 + 2\,kd1^2 + 4\,ace50\,s20 - 2\,e0\,s20 - 6\,kd1\,s20) \,/\, (4\,(2\,ace50 - e0 - 2\,kd1)) + \\
& \frac{1}{2}\sqrt{\Big((-4\,ace50^2 + 5\,ace50\,e0 - 2\,e0^2 + 2\,ace50\,kd1 - 4\,e0\,kd1 + 2\,kd1^2 + 4\,ace50\,s20 - 2\,e0\,s20 - 6\,kd1\,s20)^2 \,/\, (4\,(2\,ace50 - e0 - 2\,kd1)^2) - \frac{1}{3\,(2\,ace50 - e0 - 2\,kd1)} \\
& (-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + \\
& \Big((-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^2 + \\
& 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20) \\
& (ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)\Big) \,/\, \Big(3\,2^{1/3}\,(2\,ace50 - e0 - 2\,kd1)\Big) \\
& \Big(2\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + \\
& 108\,kd1^2\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)^2\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) - \\
& 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + \\
& 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 36\,kd1\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20) \\
& (-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) \\
& (ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3) + \\
& 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \\
& \sqrt{\Big(-4\,\Big((-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - \\
& 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - \\
& 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)\Big)^2 + \\
& \Big(2\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - \\
& 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)^2\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) - \\
& 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + \\
& 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 36\,kd1\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - \\
& 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + \\
& 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3) + 216\,(2\,ace50 - e0 - 2\,kd1) \\
& kd1^2\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2\Big)^2\Big)\Big)^{1/3}\Big) + \frac{1}{6\,2^{1/3}\,(2\,ace50 - e0 - 2\,kd1)} \\
& \Big(\Big(2\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + \\
& 108\,kd1^2\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)^2\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) - 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2 \\
& (-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) \\
& (2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 36\,kd1\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20) \\
& (-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) \\
& (ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3) + \\
& 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \\
& \sqrt{\Big(-4\,\Big((-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - \\
& 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - \\
& 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)\Big)^2 + \\
& \Big(2\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - \\
& 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)^2\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) - \\
& 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e^{-2}\,s20 + \\
& 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)\,(2\,e0^3 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 36\,kd1\,(4\,ace50^2 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - \\
& 4\,ace50\,s20 + 2\,e0\,s20 + 6\,kd1\,s20)\,(-4\,ace50^2\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + \\
& 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3) + \\
& 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^3\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2\Big)\Big)^{1/3}\Big)\Big) - \\
& \frac{1}{2}\sqrt{\Big((-4\,ace50^2 + 5\,ace50\,e0 - 2\,e0^2 + 2\,ace50\,kd1 - 4\,e0\,kd1 + 2\,kd1^2 + 4\,ace50\,s20 - 2\,e0\,s20 - 6\,kd1\,s20)^2 \,/\, (2\,(2\,ace50 - e0 - 2\,kd1)^2) -
\end{aligned}
$$

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FIG. 6A

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$$\frac{1}{3\,(2\,ace50 - e0 - 2\,kd1)}\Bigg(2\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) - \sqrt{(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^2 - 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^3\,(2\,e0^2 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 - 4\,e0\,kd1 - 2\,kd1^2 + 4\,ace50\,s20 + 2\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,s20^2)^2 + \Big(2\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 - 4\,e0\,kd1 - 2\,kd1^2 + 4\,ace50\,s20 + 2\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,s20^2)\Big)^2 + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3) + \sqrt{(-4\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(2\,e0^2 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 - 4\,e0\,kd1 - 2\,kd1^2 + 4\,ace50\,s20 + 2\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,s20^2)^2 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \Big(2\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \frac{1}{6\,2^{1/3}\,(2\,ace50 - e0 - 2\,kd1)}\Big(2\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \sqrt{(-4\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(2\,e0^2 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 + 4\,ace50\,s20 + 2\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,s20^2)^2 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \Big(2\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \sqrt{(-4\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(2\,e0^2 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 + 4\,ace50\,s20 + 2\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,s20^2)^2 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \Big(2\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \sqrt{(-4\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 24\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(2\,e0^2 - 9\,e0^2\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 12\,kd1\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 + 4\,ace50\,s20 + 2\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,s20^2)^2 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 + 6\,ace50\,e0\,kd1 - 4\,e0^2\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2 + \frac{1}{6\,2^{1/3}\,(2\,ace50 - e0 - 2\,kd1)}\Big(2\,(-4\,ace50^4\,e0 + 6\,ace50\,e0^3 - 2\,e0^4 + 6\,ace50\,e0^3\,kd1 - 4\,e0^4\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^3\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^3\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2)^3 + 108\,kd1^2\,(4\,ace50^3 - 5\,ace50\,e0 + 2\,e0^2 - 2\,ace50\,kd1 + 4\,e0\,kd1 - 2\,kd1^2 - 4\,ace50\,s20 + 2\,e0\,s20 + 12\,e0\,s20^2 - 4\,s20^3) + 144\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(-4\,ace50^3\,e0 + 6\,ace50\,e0^2 - 2\,e0^3 + 6\,ace50\,e0^2\,kd1 - 4\,e0^3\,kd1 + 10\,e0\,kd1^2 + 8\,ace50^2\,s20 - 14\,ace50\,e0\,s20 + 5\,e0^2\,s20 + 2\,e0\,kd1\,s20 + 4\,kd1^2\,s20 + 4\,ace50\,s20^2 - 2\,e0\,s20^2 - 12\,kd1\,s20^2) + 216\,(2\,ace50 - e0 - 2\,kd1)\,kd1^2\,(ace50\,e0^2 + 4\,e0^2\,kd1 - ace50\,e0\,s20 - 2\,e0^2\,s20 - 7\,e0\,kd1\,s20 - 2\,ace50\,s20^2 + 5\,e0\,s20^2 - 2\,kd1\,s20^2 - 2\,s20^3)^2\Big)^{1/3}\Big)\Bigg)$$

FIG. 6B

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FIG. 6C

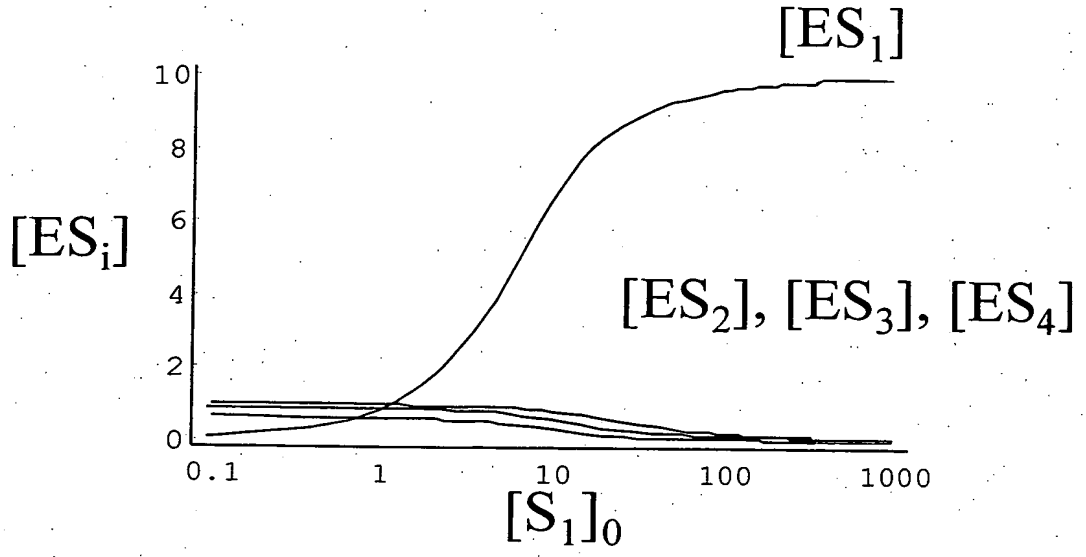


FIG. 7

$K_{d1} = 1\,\mu M$

$K_{d2} = 0.5$

$K_{d3} = 2$

$K_{d4} = 5$

$[S_1]$ = variable

$[S_2]_0 = [S_3]_0 = [S_4]_0 = 1$

$[E]_0 = 10$

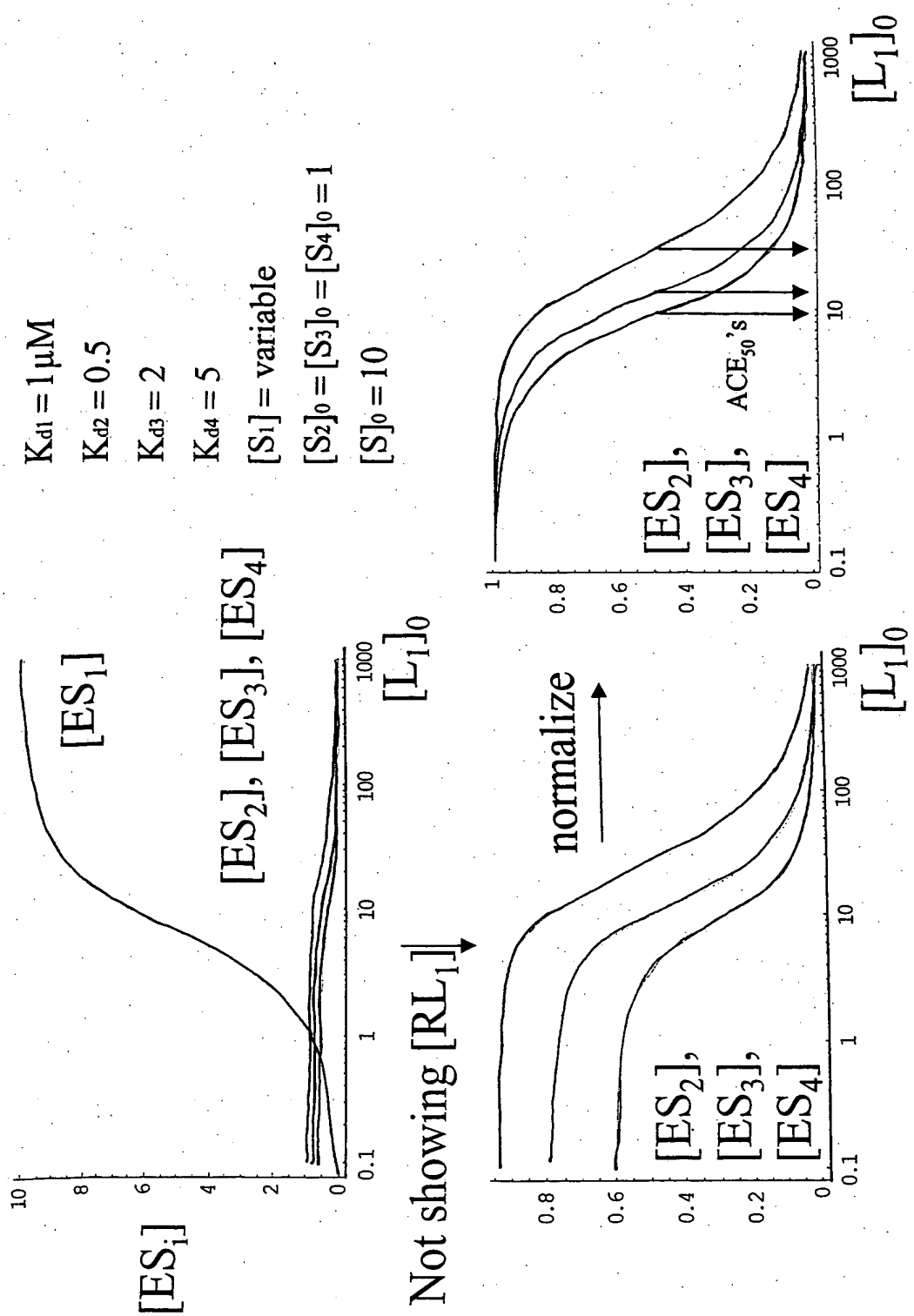

$K_{d1} = 1\,\mu M$
$K_{d2} = 0.5$
$K_{d3} = 2$
$K_{d4} = 5$
$[S_1]$ = variable
$[S_2]_0 = [S_3]_0 = [S_4]_0 = 1$
$[S]_0 = 10$
$[ES_1]$
$[ES_2]$, $[ES_3]$, $[ES_4]$
$[ES_i]$
$[L_1]_0$
Not showing $[RL_1]$
normalize
$[ES_2]$, $[ES_3]$, $[ES_4]$
ACE_{50}'s

FIG. 8

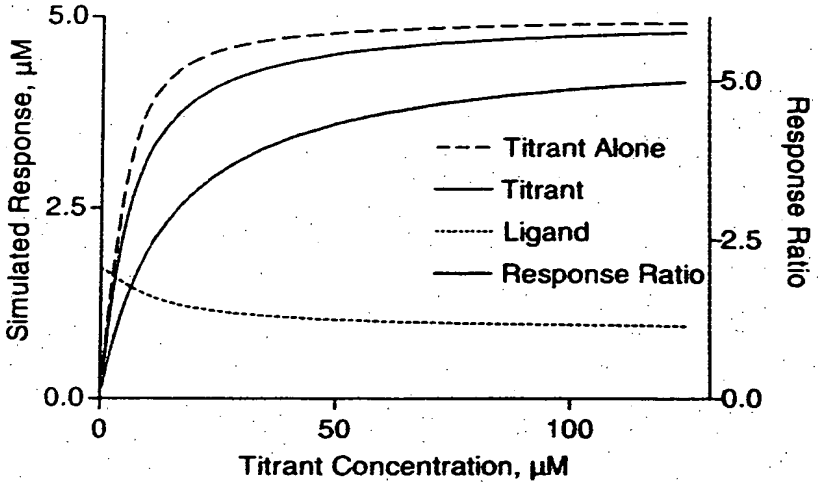

5.0
2.5
0.0
Simulated Response, µM
0
50
100
Titrant Concentration, µM
Titrant Alone
Titrant
Ligand
Response Ratio
5.0
2.5
0.0
Response Ratio

FIG. 9

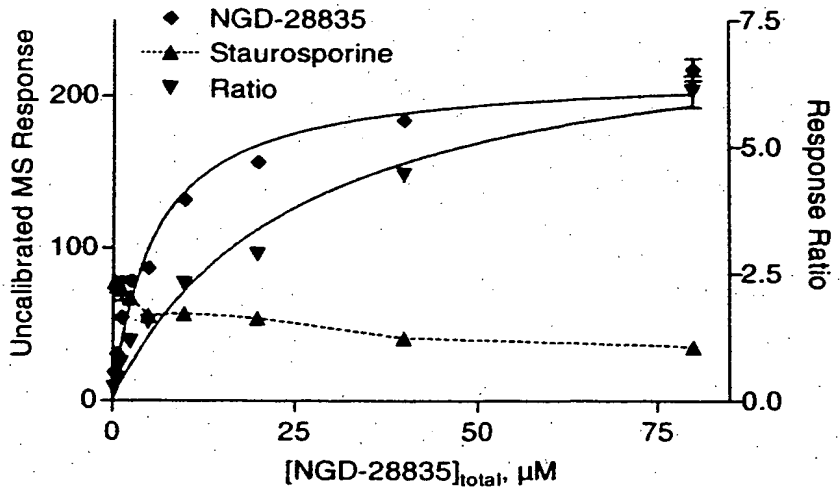

NGD-28835
Staurosporine
Ratio
200
100
0
Uncalibrated MS Response
0
25
50
75
[NGD-28835]total, µM
7.5
5.0
2.5
0.0
Response Ratio

FIG. 10

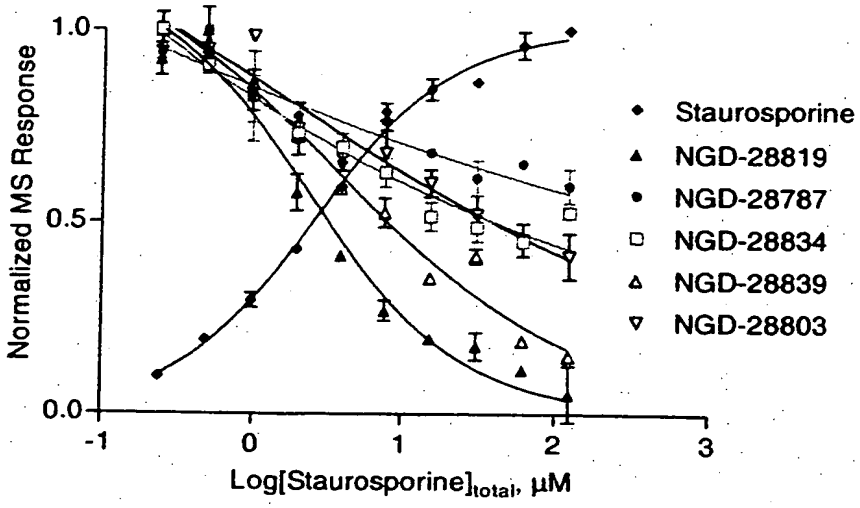


FIG. 11A

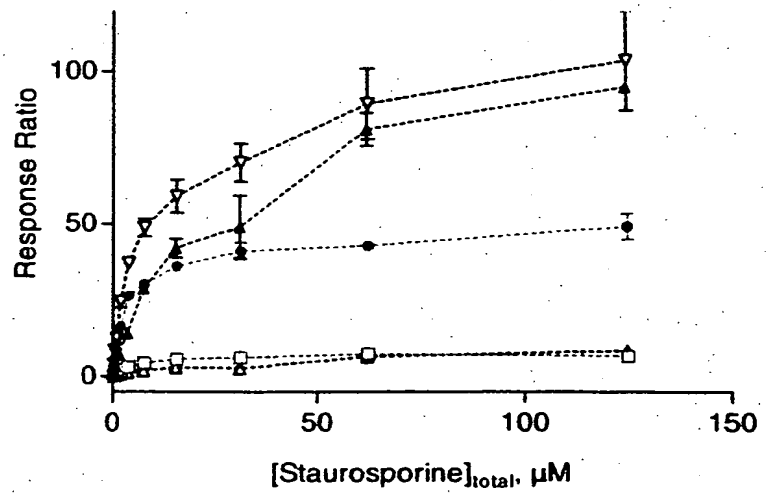


FIG. 11B

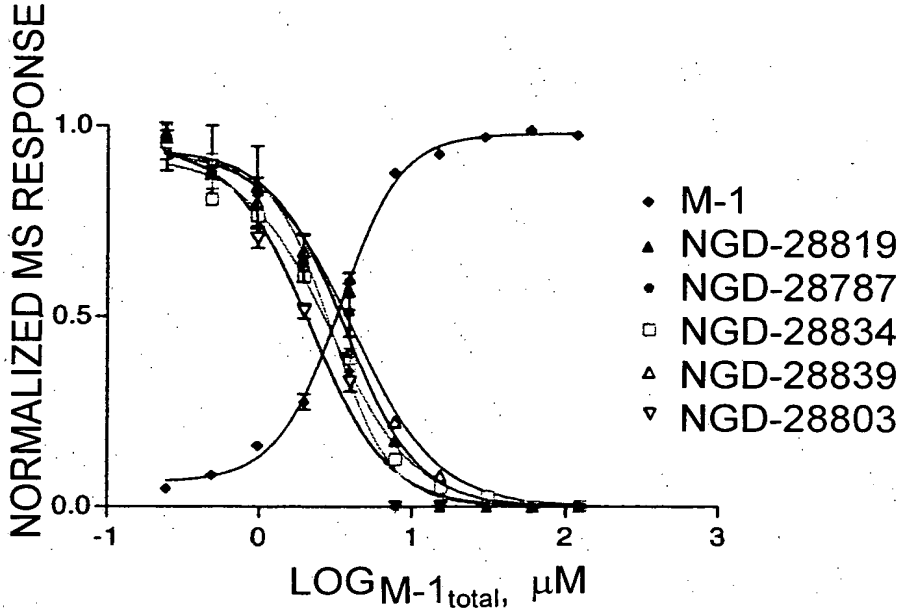


FIG. 11C

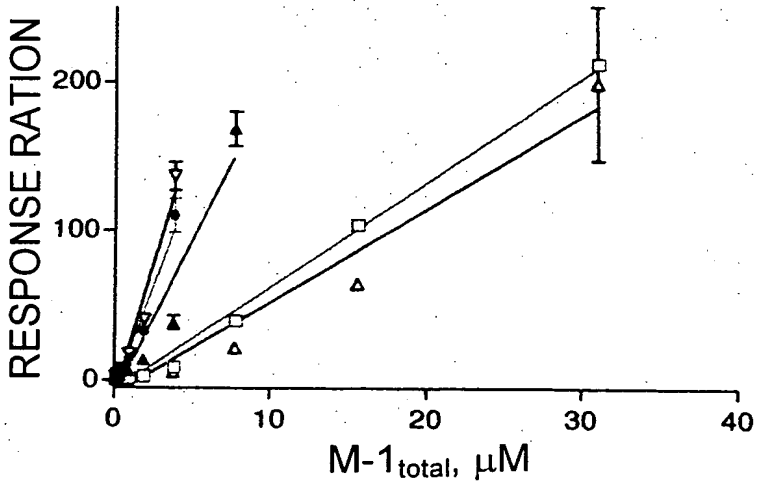


FIG. 11D

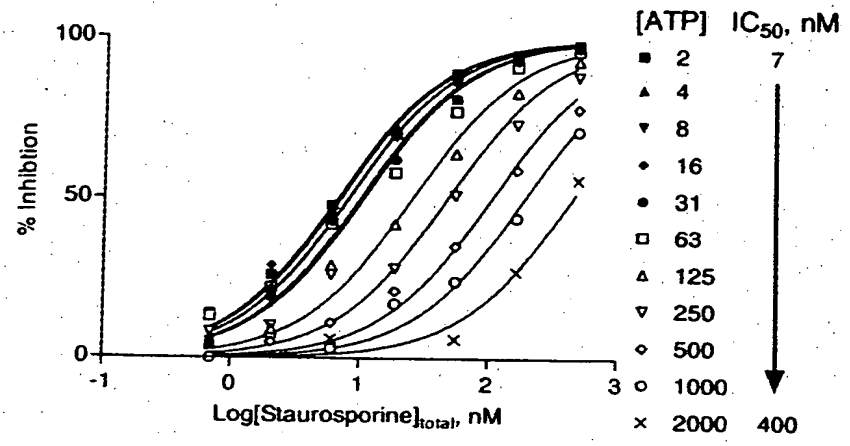


FIG. 12A

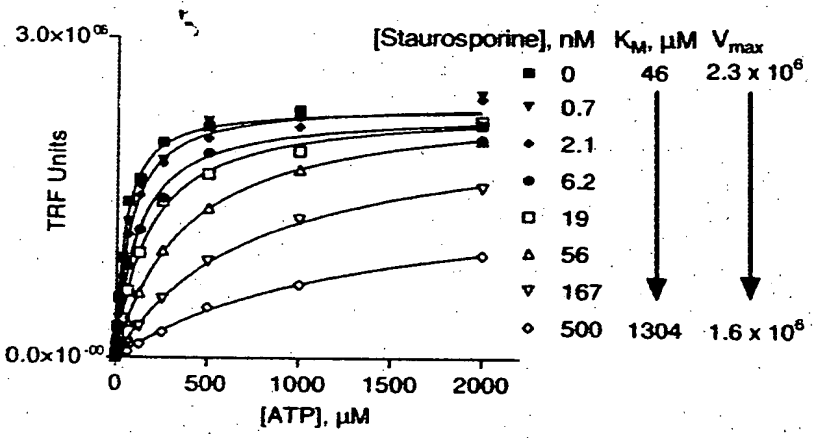


FIG. 12B

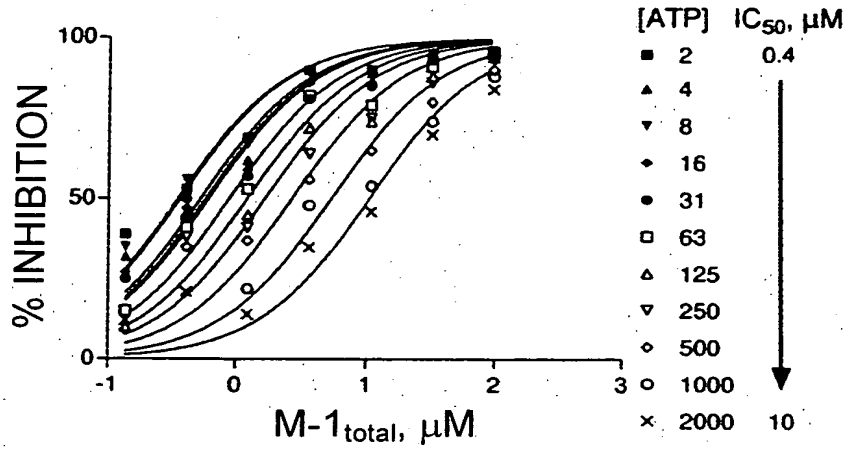


FIG. 12C

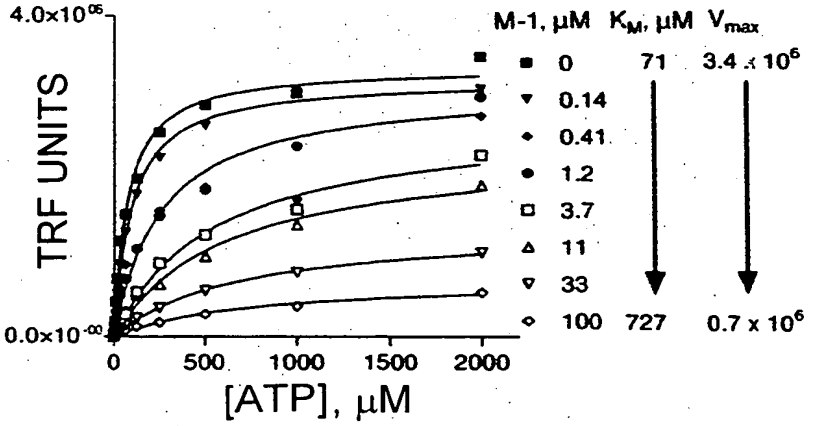


FIG. 12D

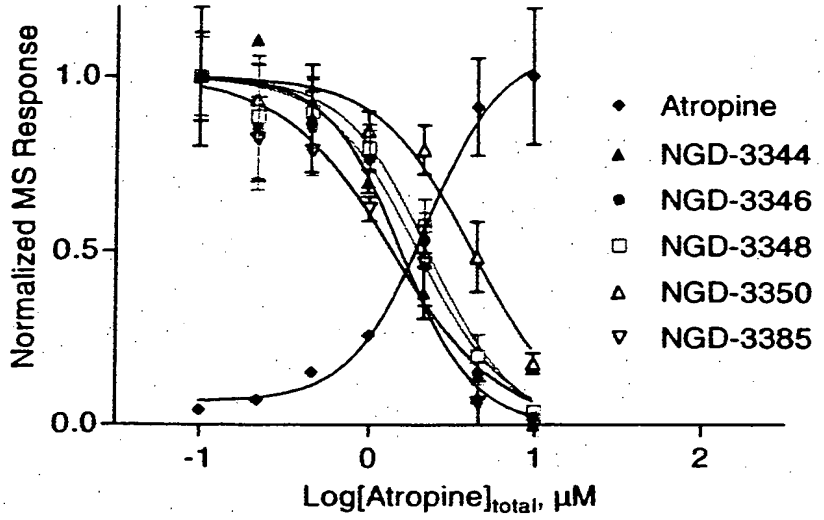


FIG. 13A

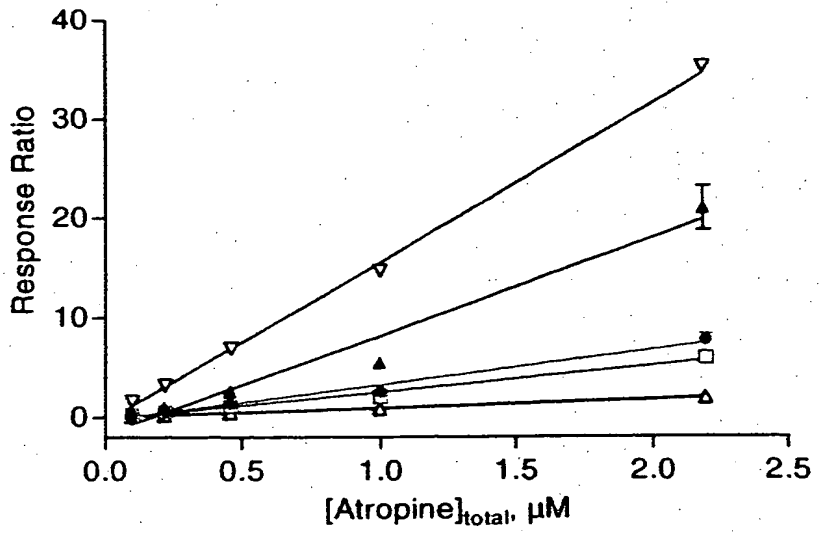


FIG. 13B

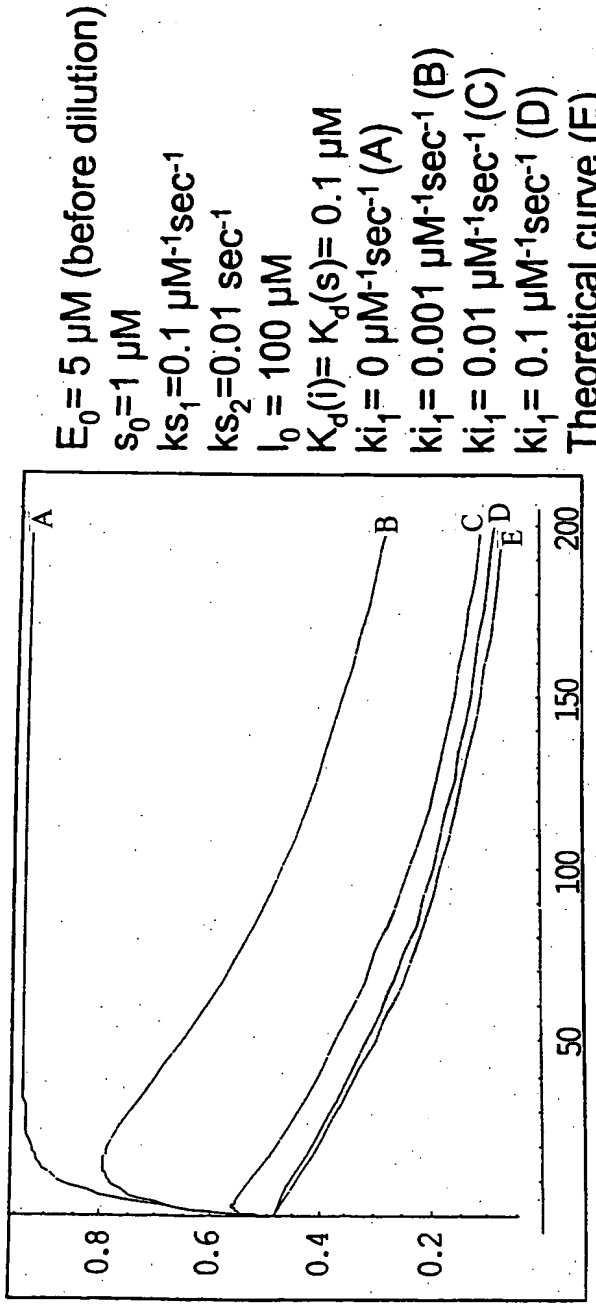

E_0= 5 µM (before dilution)
s_0=1 µM
ks_1=0.1 µM^{-1}sec^{-1}
ks_2=0.01 sec^{-1}
I_0 = 100 µM
$K_d(i)$= $K_d(s)$= 0.1 µM
ki_1= 0 µM^{-1}sec^{-1} (A)
ki_1= 0.001 µM^{-1}sec^{-1} (B)
ki_1= 0.01 µM^{-1}sec^{-1} (C)
ki_1= 0.1 µM^{-1}sec^{-1} (D)
Theoretical curve (E)
A
B
C
D
E
0.8
0.6
0.4
0.2
50
100
150
200
[E·S]
Time, sec

FIG. 14

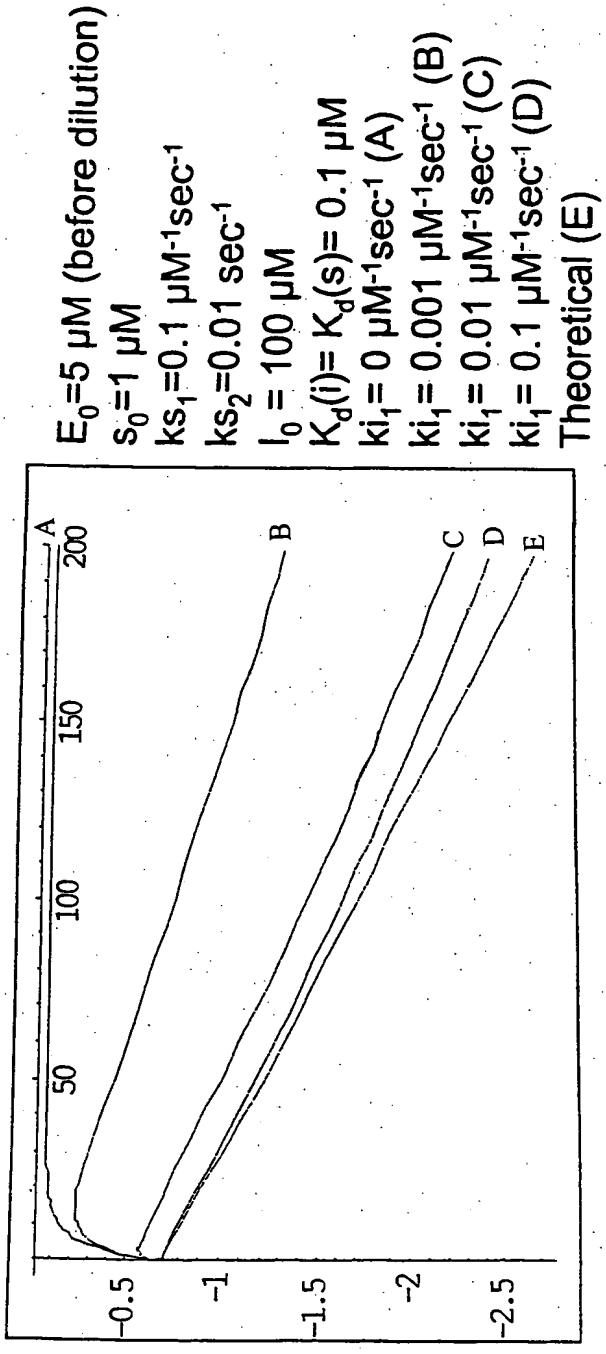

E_0=5 µM (before dilution)
s_0=1 µM
ks_1=0.1 µM^{-1}sec^{-1}
ks_2=0.01 sec^{-1}
I_0 = 100 µM
$K_d(i)$= $K_d(s)$= 0.1 µM
ki_1= 0 µM^{-1}sec^{-1} (A)
ki_1= 0.001 µM^{-1}sec^{-1} (B)
ki_1= 0.01 µM^{-1}sec^{-1} (C)
ki_1= 0.1 µM^{-1}sec^{-1} (D)
Theoretical (E)
A
B
C
D
E
50
100
150
200
-0.5
-1
-1.5
-2
-2.5
Ln[E·S]
Time, sec

FIG. 15

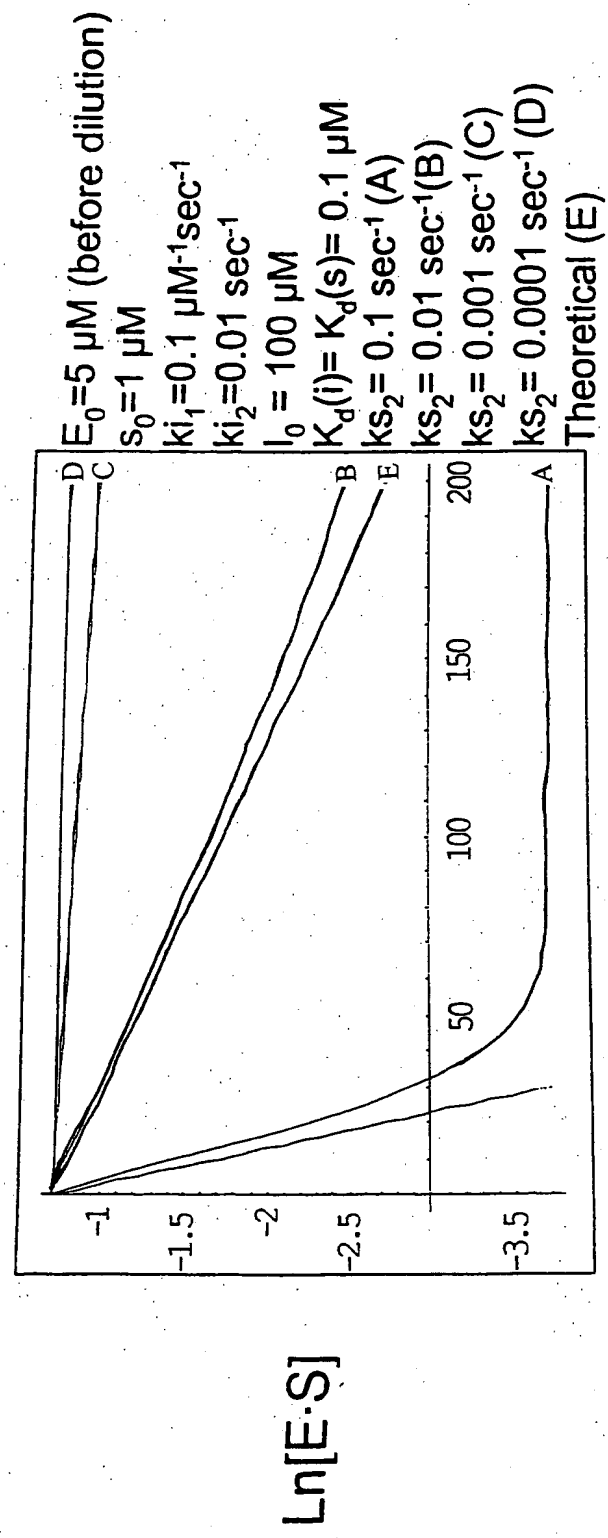

E_0=5 µM (before dilution)
s_0=1 µM
ki_1=0.1 µM^{-1}sec^{-1}
ki_2=0.01 sec^{-1}
I_0 = 100 µM
$K_d(i) = K_d(s)$= 0.1 µM
ks_2= 0.1 sec^{-1} (A)
ks_2= 0.01 sec^{-1}(B)
ks_2= 0.001 sec^{-1}(C)
ks_2= 0.0001 sec^{-1} (D)
Theoretical (E)
D
C
B
E
A
-1
-1.5
-2
-2.5
-3.5
50
100
150
200
Ln[E·S]
Time, sec

FIG. 16

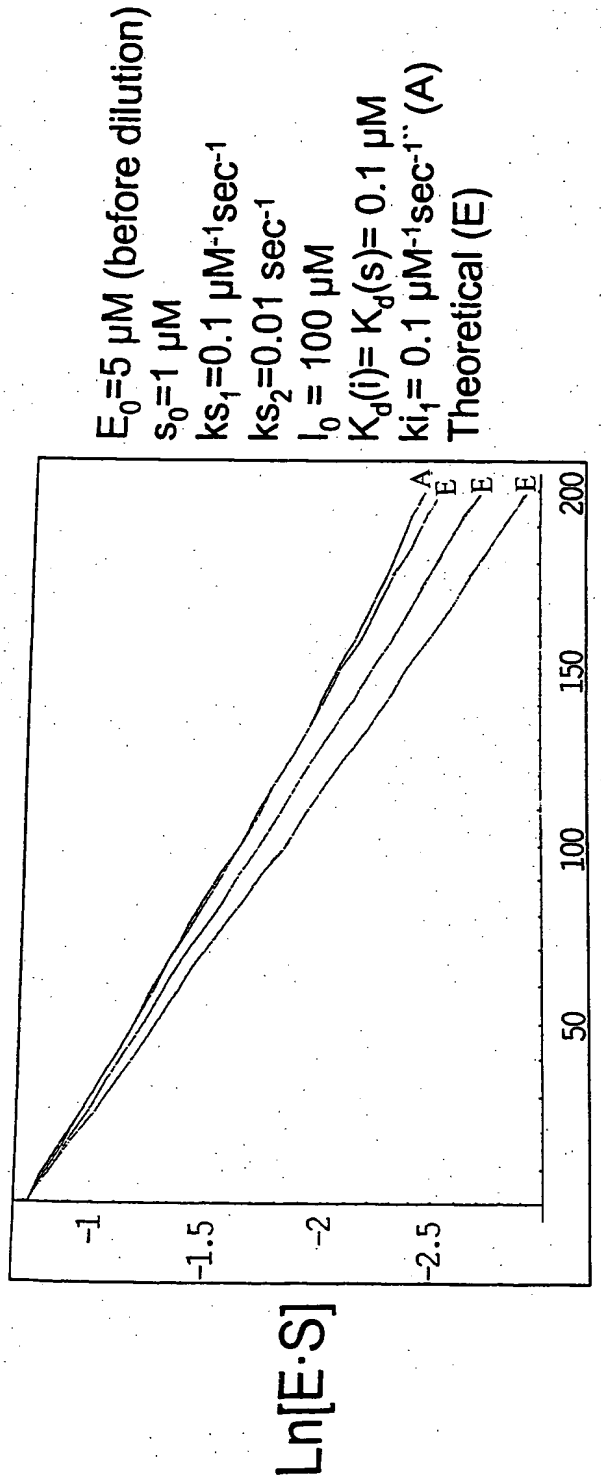

E_0=5 µM (before dilution)
s_0=1 µM
ks_1=0.1 µM^{-1}sec^{-1}
ks_2=0.01 sec^{-1}
I_0 = 100 µM
$K_d(I) = K_d(s)$= 0.1 µM
ki_1= 0.1 µM^{-1}sec^{-1} (A)
Theoretical (E)
A
E
E
E
-1
-1.5
-2
-2.5
50
100
150
200
Ln[E·S]
Time, sec

FIG. 17

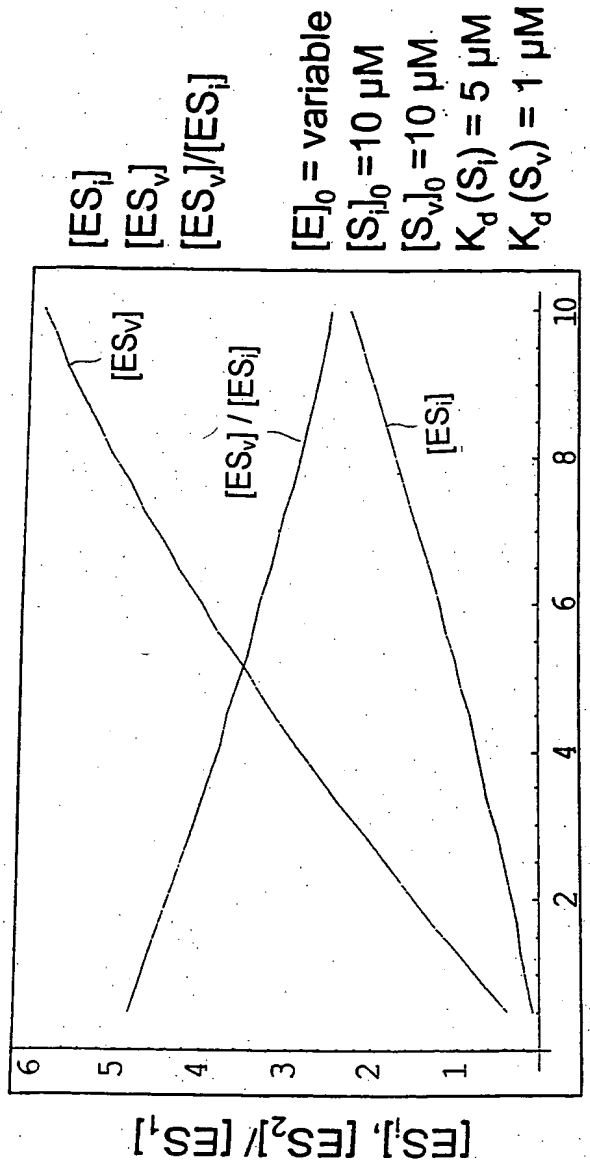

[ESi]
[ESv]
[ESv]/[ESi]
[E]0 = variable
[Si]0 =10 µM
[Sv]0 =10 µM
Kd (Si) = 5 µM
Kd (Sv) = 1 µM
[ESv]
[ESv] / [ESi]
[ESi]
[ES1], [ES2]/ [ES1]
[E]0, µM
1
2
3
4
5
6
2
4
6
8
10

FIG. 18

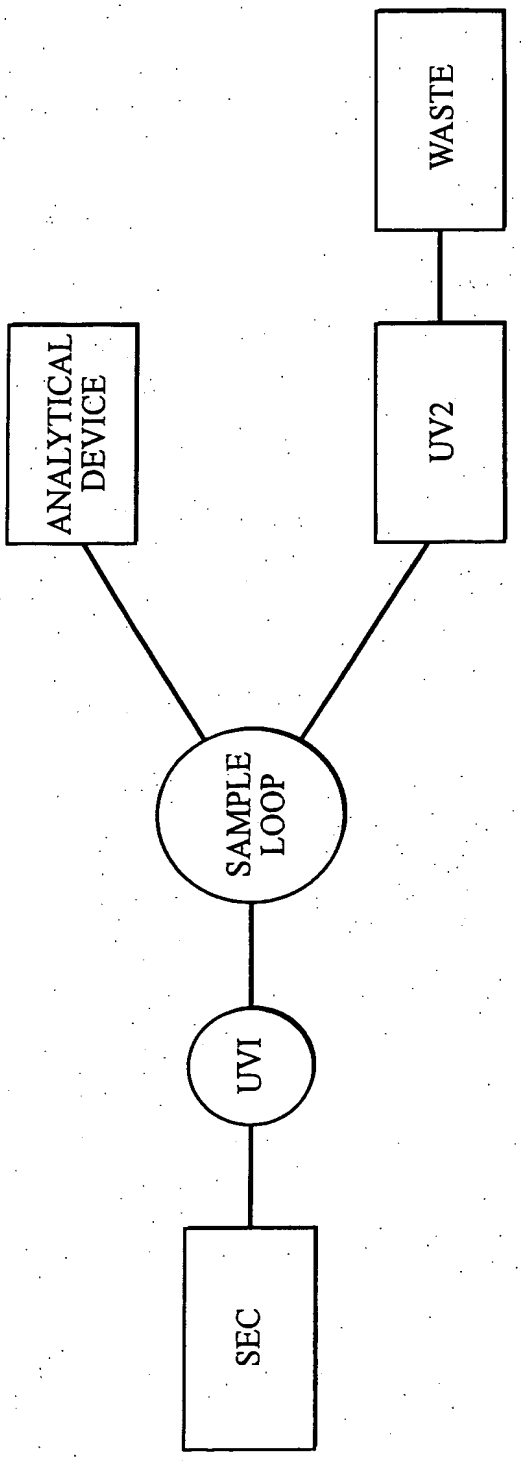


FIG. 19

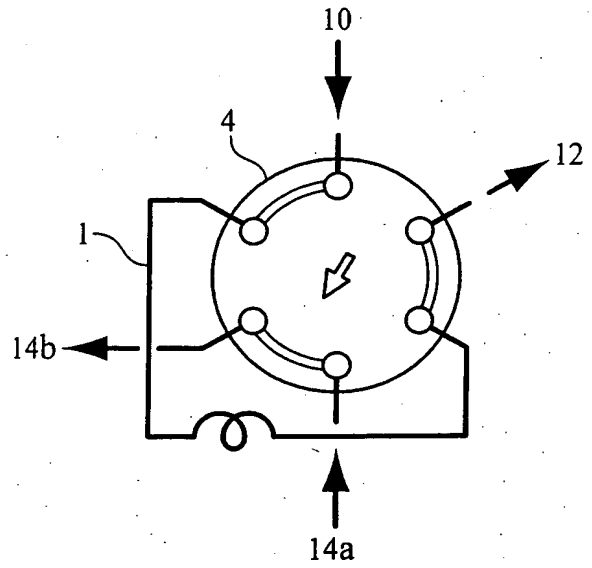


FIG. 20A

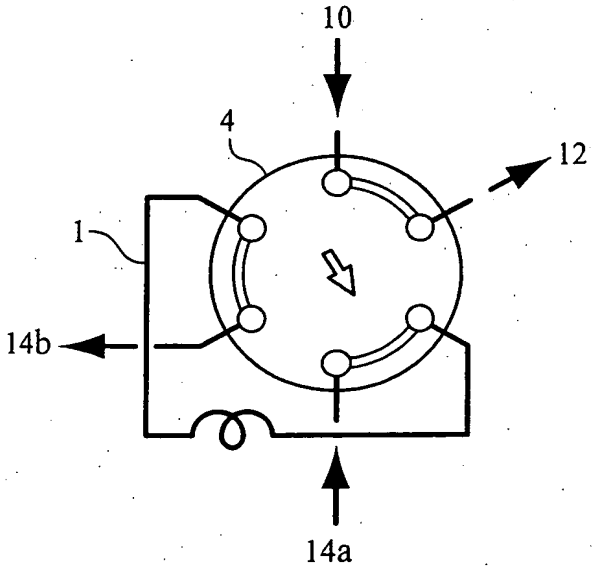


FIG. 20B

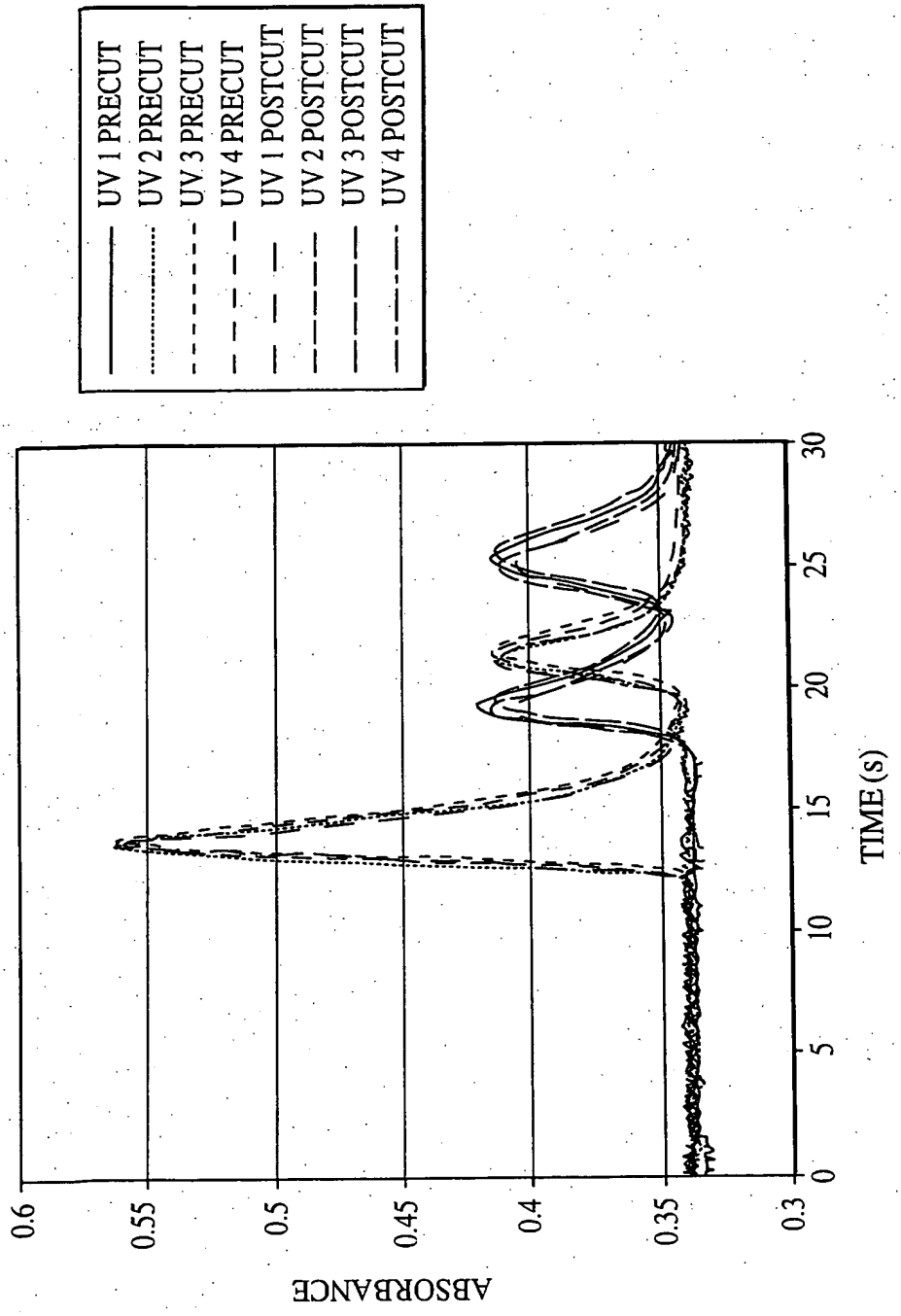

UV 1 PRECUT
UV 2 PRECUT
UV 3 PRECUT
UV 4 PRECUT
UV 1 POSTCUT
UV 2 POSTCUT
UV 3 POSTCUT
UV 4 POSTCUT
ABSORBANCE
0.6
0.55
0.5
0.45
0.4
0.35
0.3
TIME (s)
0
5
10
15
20
25
30

FIG. 21

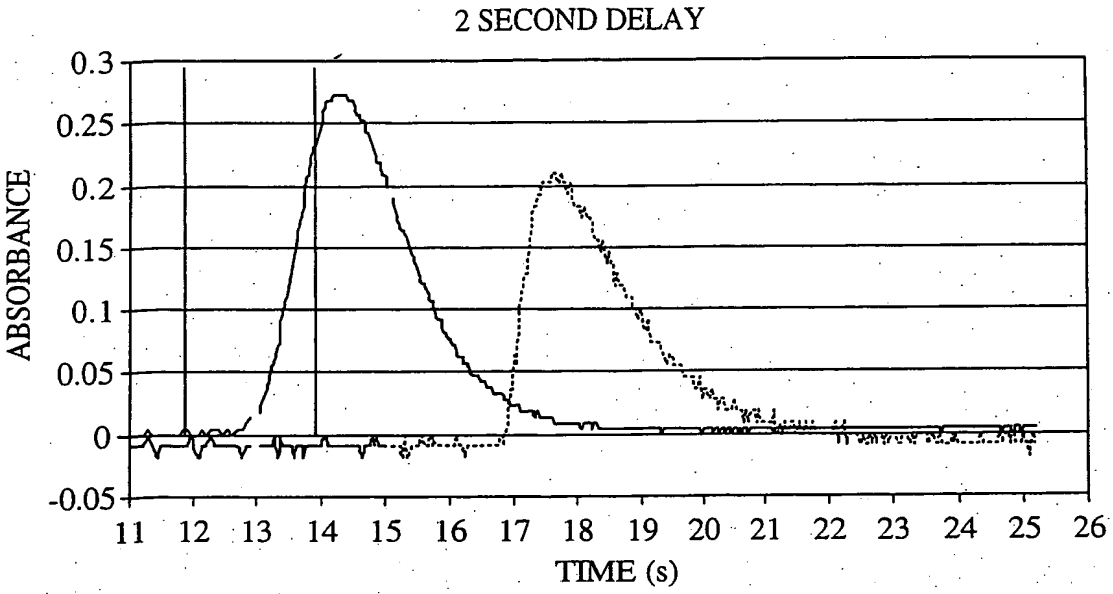


FIG. 22A

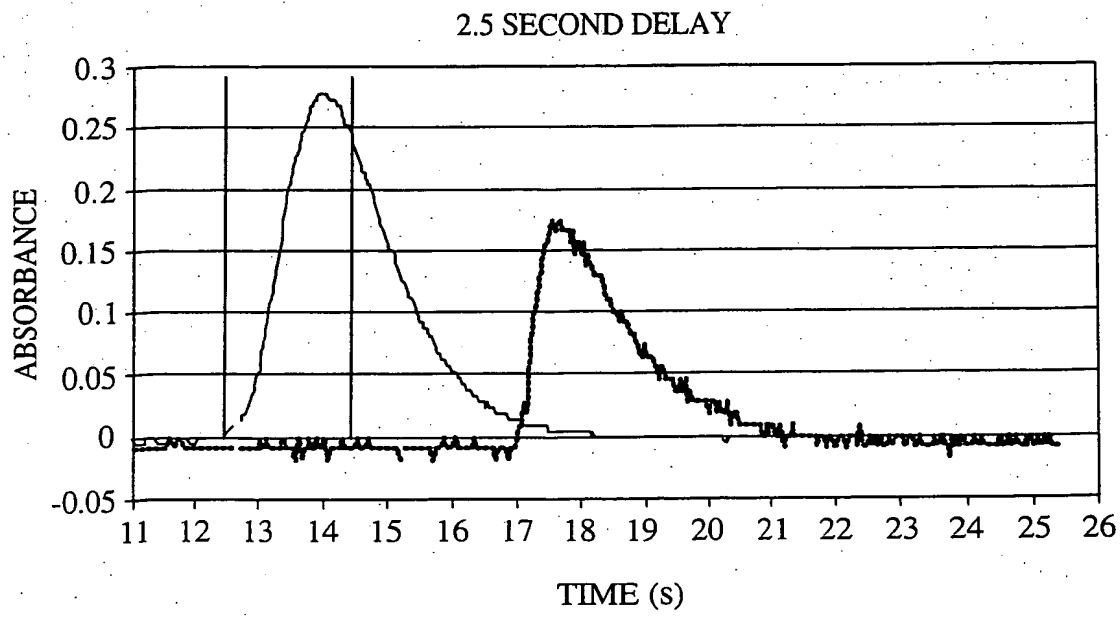


FIG. 22B

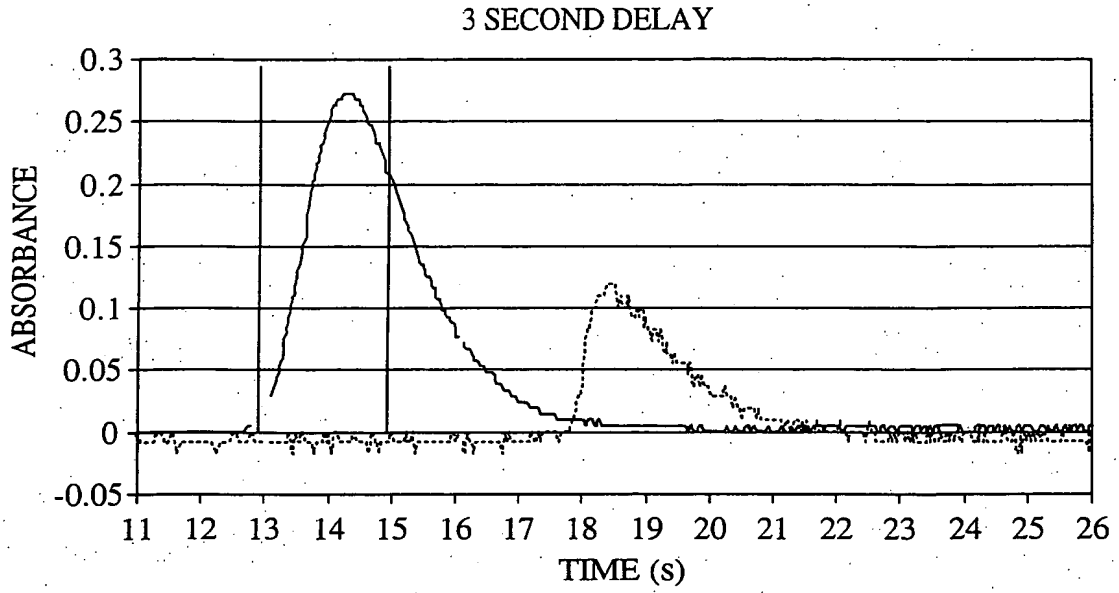


FIG. 22C

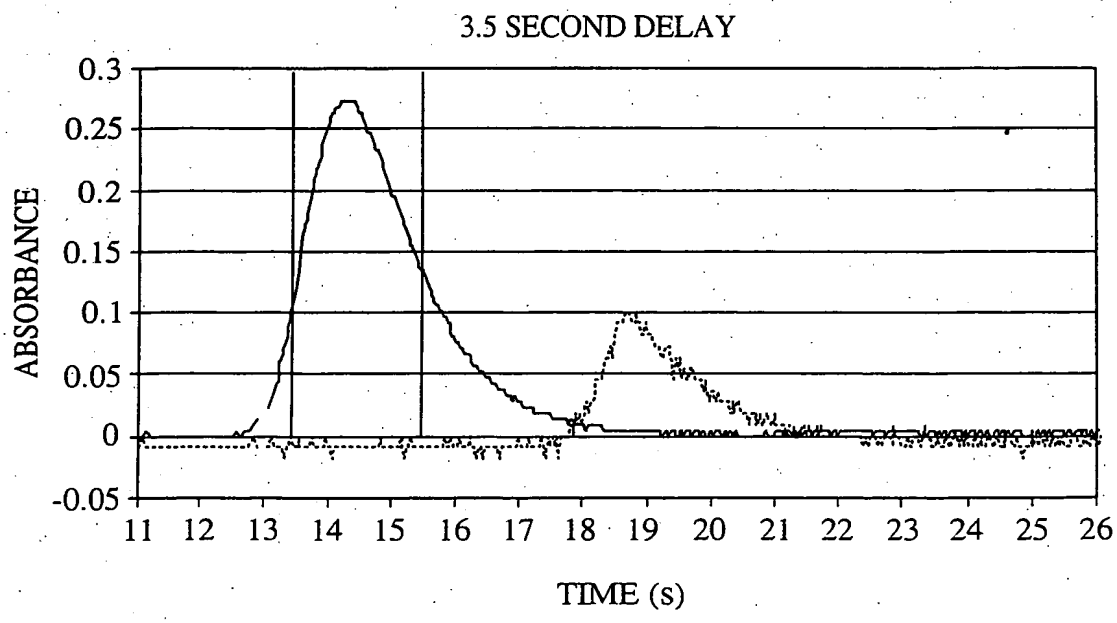


FIG. 22D

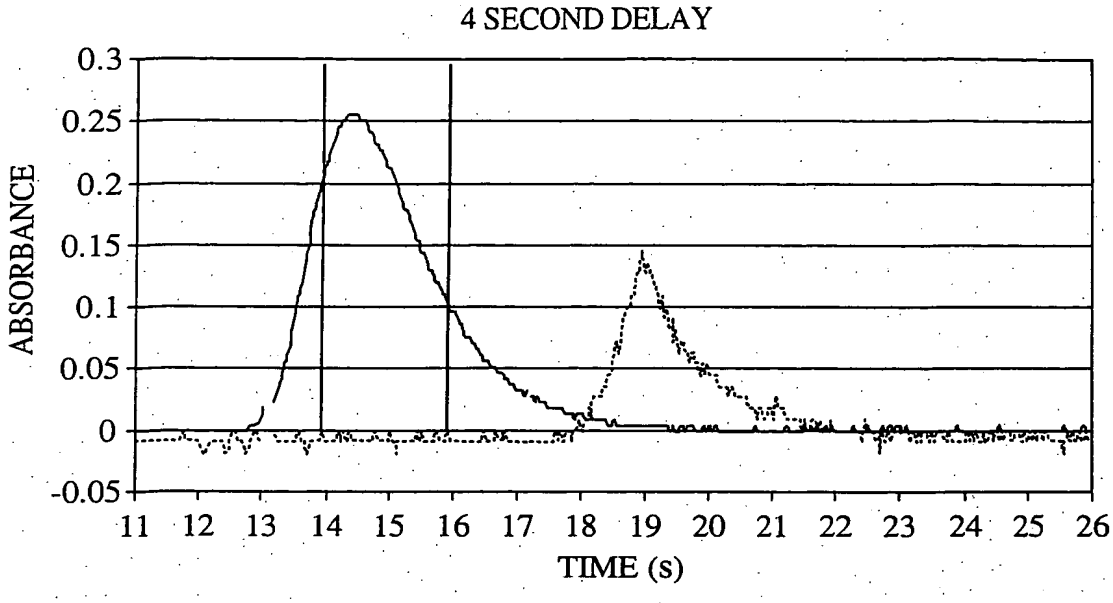


FIG. 22E

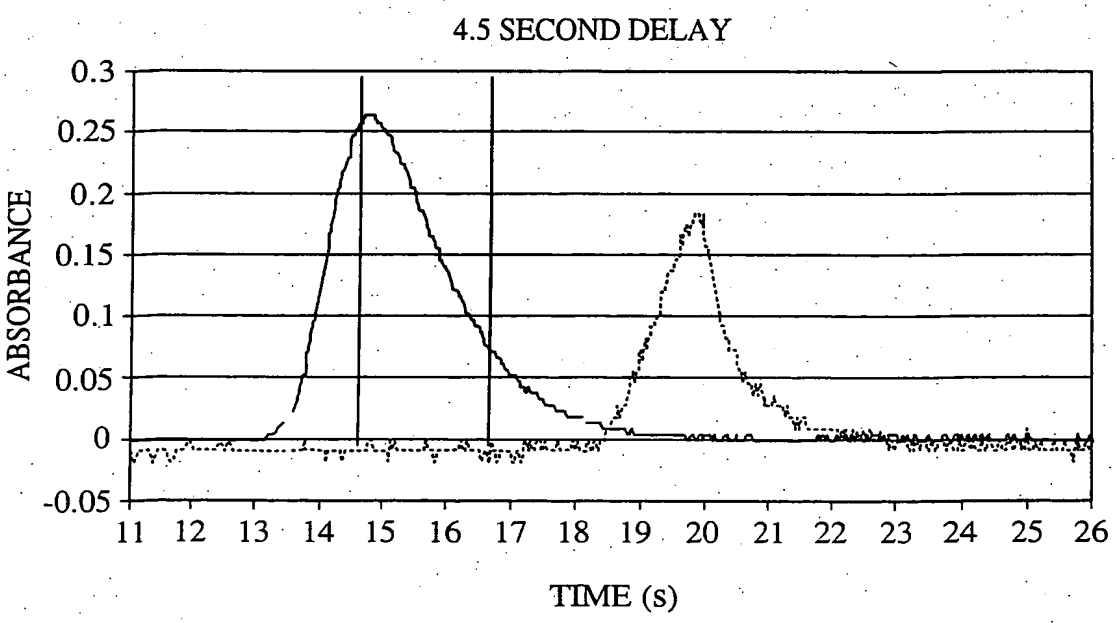


FIG. 22F

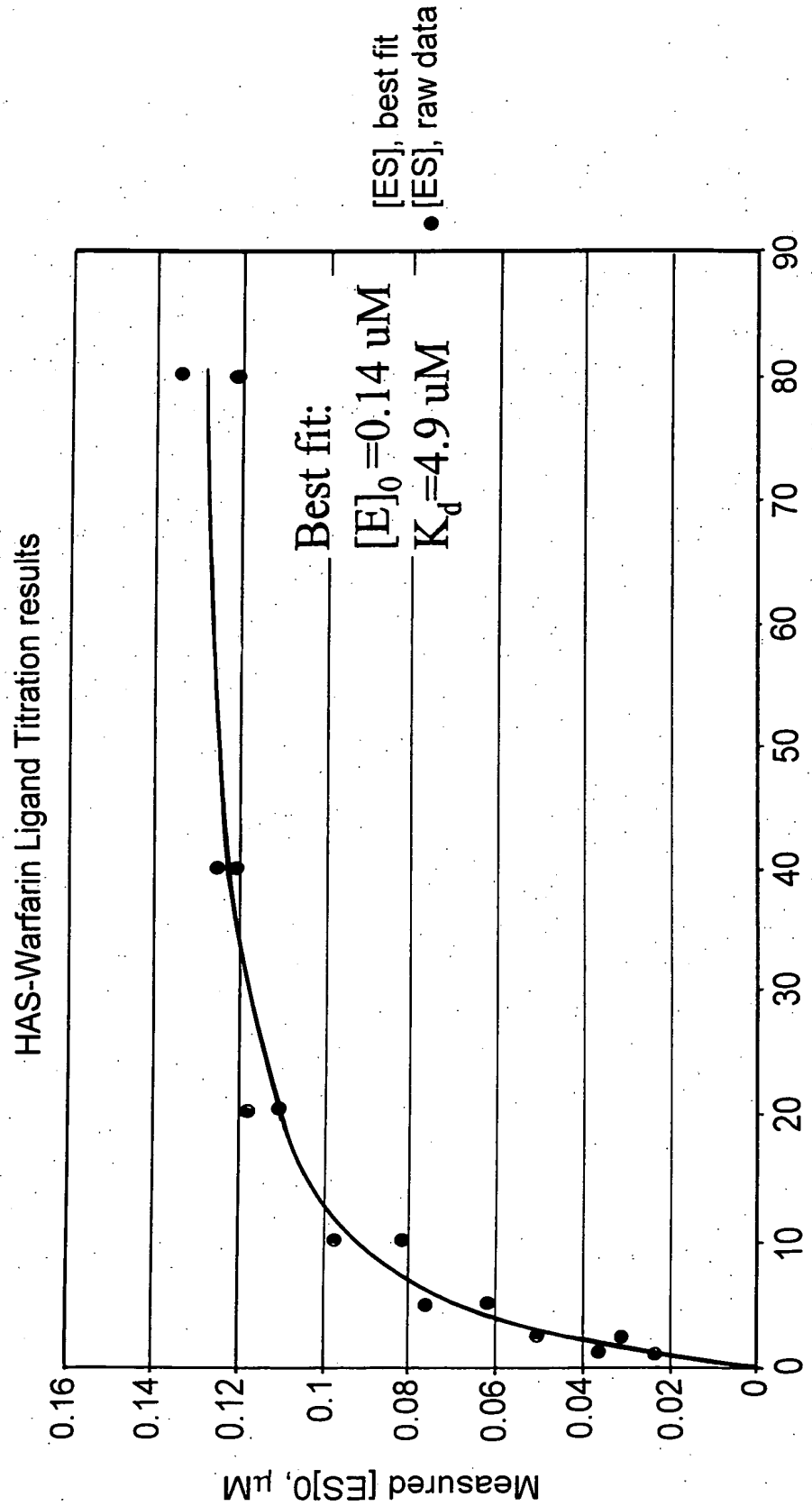

HAS-Warfarin Ligand Titration results
Best fit:
$[E]_0$ =0.14 uM
K_d=4.9 uM
[ES], best fit
[ES], raw data
Measured [ES]0, µM
Initial [ligand], µM
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
10
20
30
40
50
60
70
80
90

FIG. 23

	ACE50, μM
Atropine	2.2
NGD-3344	1.8
NGD-3346	2.6
NGD-3348	2.7
NGD-3350	7.1
NGD-3385	2.3

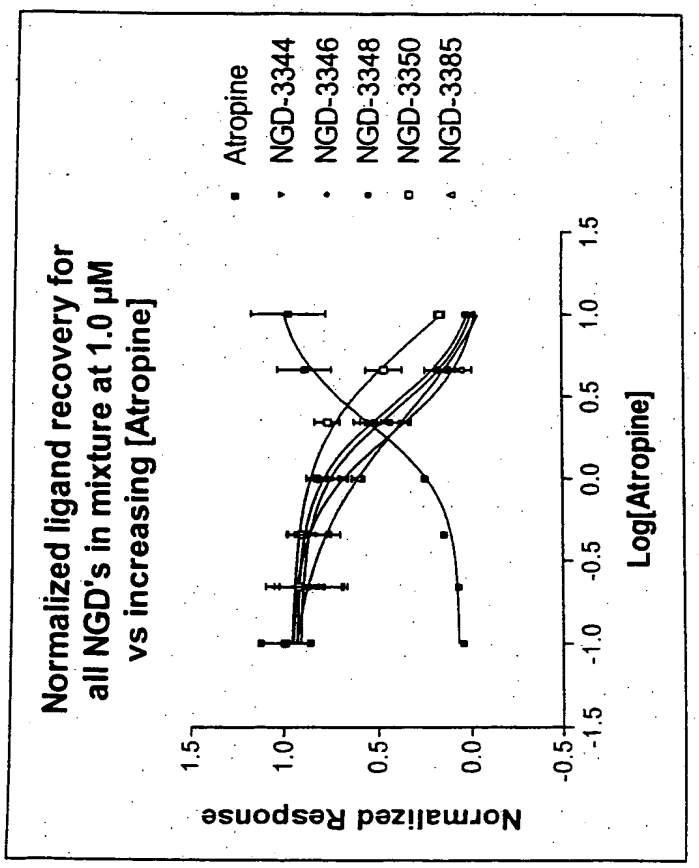
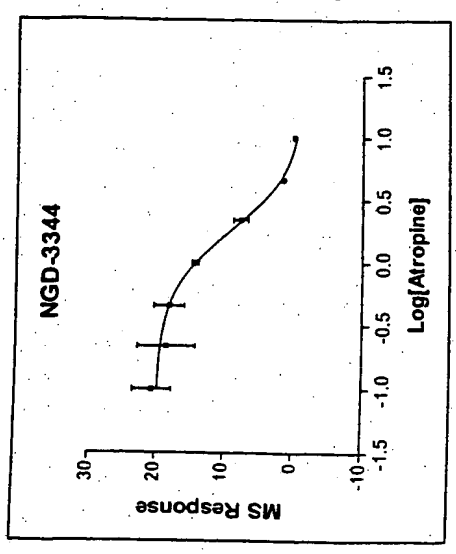


FIG. 24

- Comparison of NGD-3344 (weak) and NGD-3350 (strong) ligands shown
- K_d of ligands in mixture calculated from ACE_{50} given K_d of inhibitor (0.010 μM) & protein concentration = 2.0 μM

	ACE50, μM	Kd, μM
NGD-3344	1.8	0.75
NGD-3346	2.6	0.20
NGD-3348	2.7	0.19
NGD-3350	7.1	0.03
NGD-3385	2.3	0.30



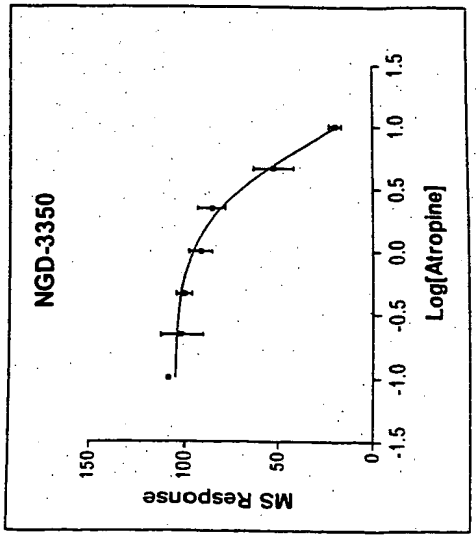


FIG. 25

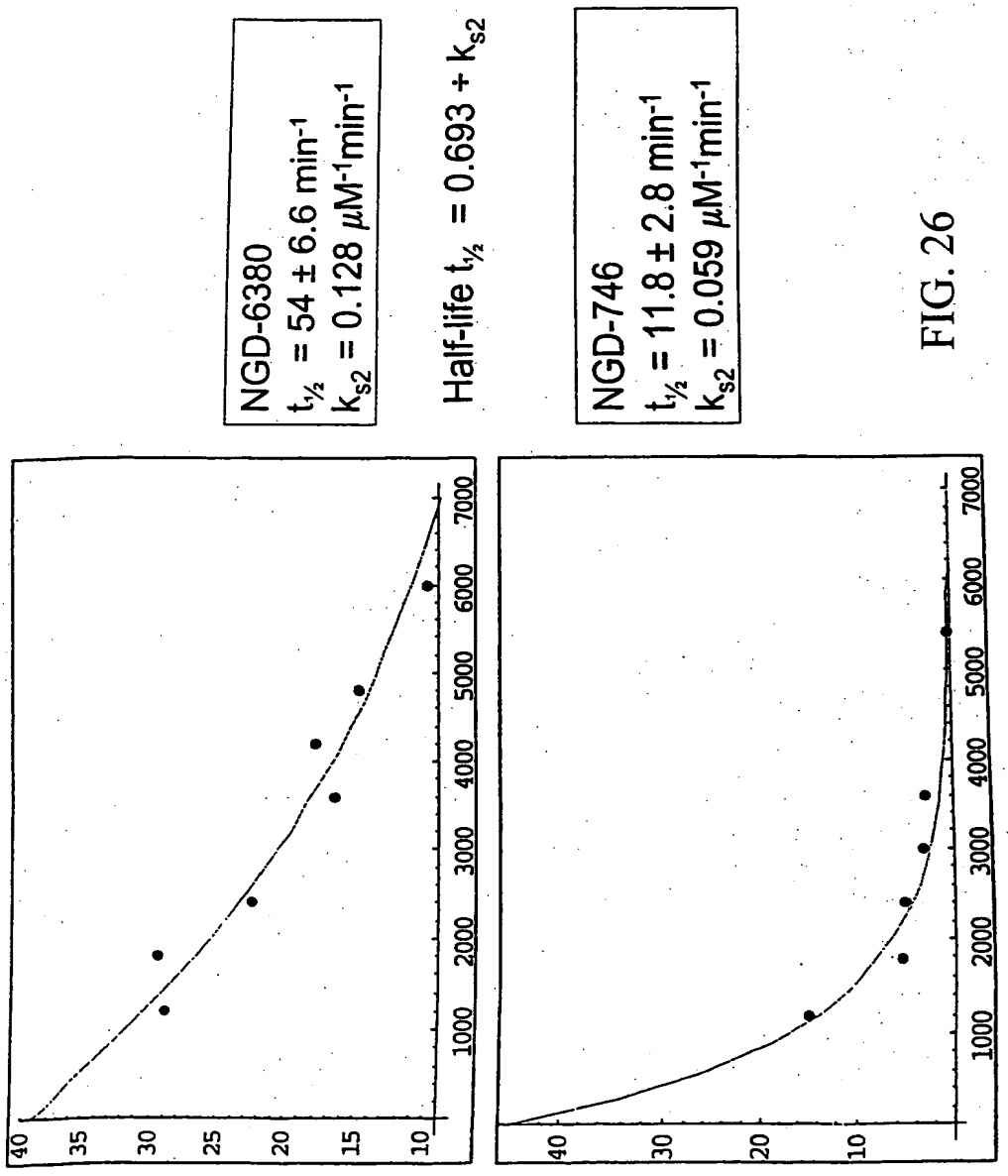
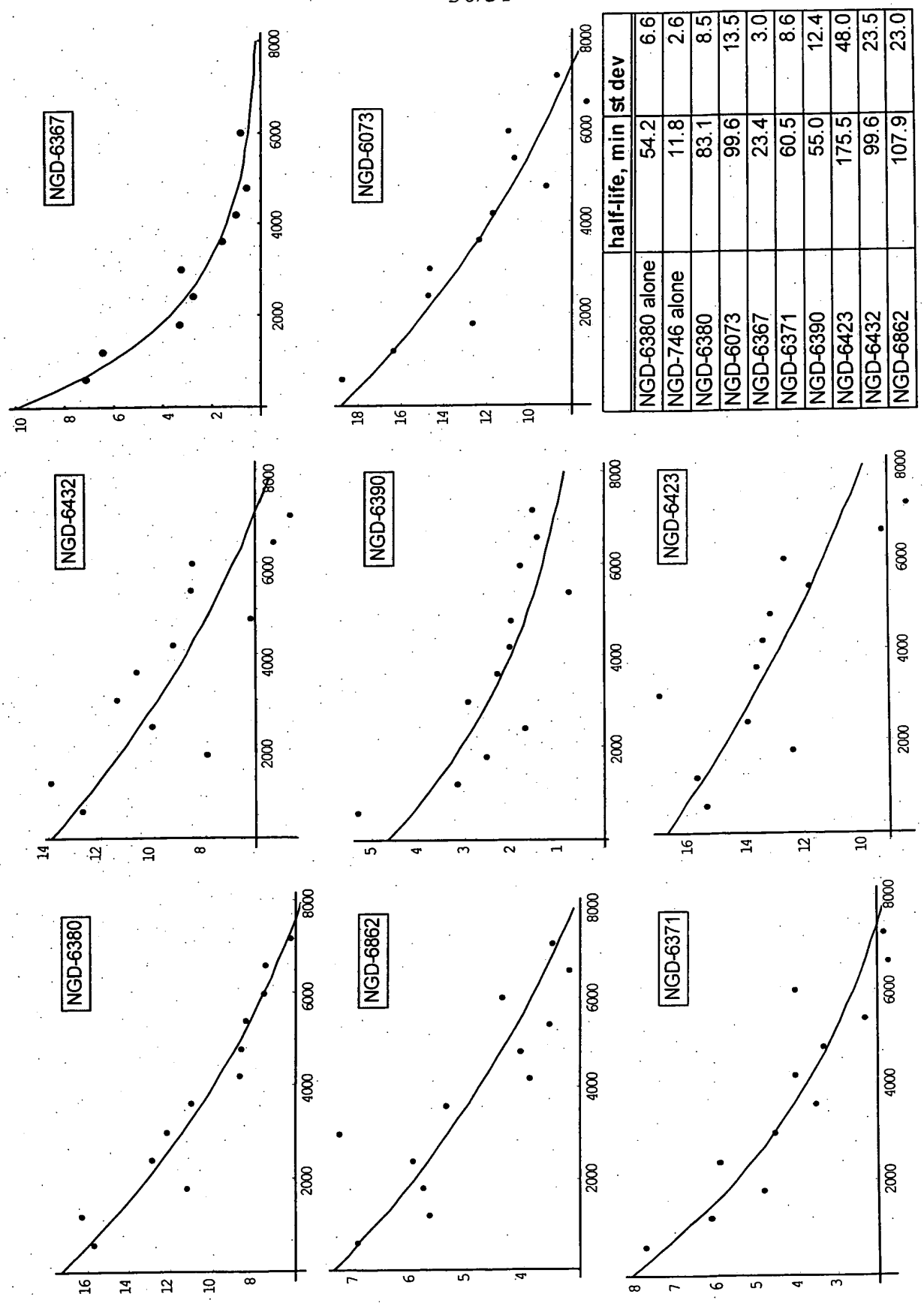

NGD-6380
$t_{½}$ = 54 ± 6.6 min^{-1}
k_{s2} = 0.128 μM^{-1}min^{-1}
Half-life $t_{½}$ = 0.693 + k_{s2}
NGD-746
$t_{½}$ = 11.8 ± 2.8 min^{-1}
k_{s2} = 0.059 μM^{-1}min^{-1}
40
35
30
25
20
15
10
1000
2000
3000
4000
5000
6000
7000

FIG. 26



	half-life, min	st dev
NGD-6380 alone	54.2	6.6
NGD-746 alone	11.8	2.6
NGD-6380	83.1	8.5
NGD-6073	99.6	13.5
NGD-6367	23.4	3.0
NGD-6371	60.5	8.6
NGD-6390	55.0	12.4
NGD-6423	175.5	48.0
NGD-6432	99.6	23.5
NGD-6862	107.9	23.0

FIG. 27

	ACE50, µM	Kd, nM
NGD-6380	3.27	27
NGD-6862	n/d	
NGD-6371	3.03	30
NGD-6432	1.93	53
NGD-6390	3.04	29
NGD-6423	2.69	34
NGD-6367	2.44	39
NGD-6073	1.93	52
NGD-746	0.58	500

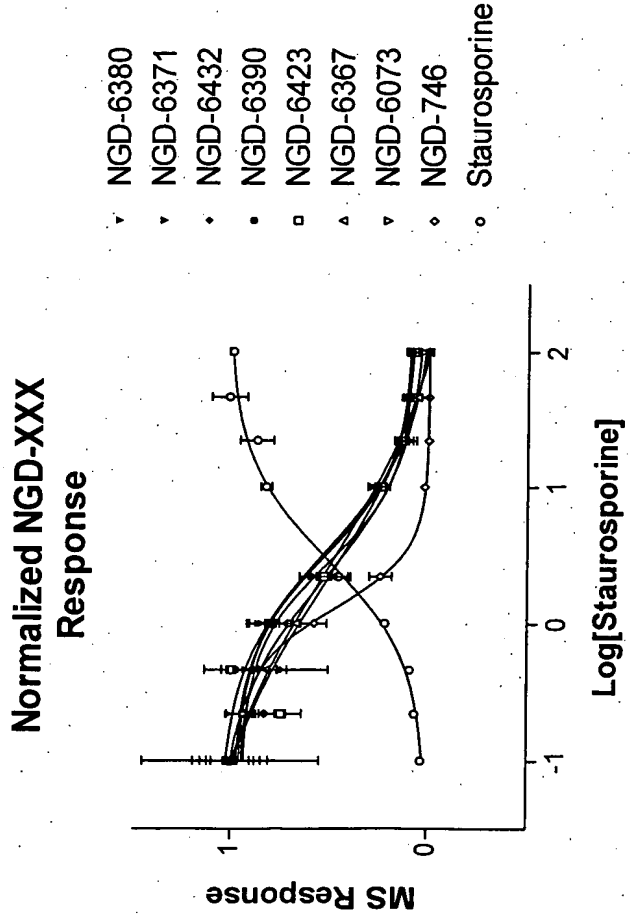


FIG. 28